



Benign approach for methyl-esterification of oxygenated organic compounds using TBHP as methylating and oxidizing agent

Topi Ghosh^a, Prakash Chandra^b, Akbar Mohammad^a, Shaikh M. Mobin^{a,b,c,*}

^a Discipline of Chemistry, Indian Institute of Technology Indore, Simrol, Khandwa Road, Indore, 453552, India

^b Discipline of Metallurgy Engineering and Material Science, Indian Institute of Technology Indore, Simrol, Khandwa Road, Indore, 453552, India

^c Discipline of Biosciences and Bio-Medical Engineering, Indian Institute of Technology Indore, Simrol, Khandwa Road, Indore, 453552, India

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ABSTRACT

Methyl-esterification of oxygenates such as alcohols, aldehydes and carboxylic acids were carried out by employing copper and copper/palladium based catalysts using TBHP. In this reaction, TBHP plays dual role as oxidizing and methylating agent. Cu and Cu-Pd based nanoparticles (NPs) were prepared by wet chemical method using CuCl or PdCl₂ by engaging “green solvent” water and dextrose as eco-friendly and renewable reagents. The NPs were fully characterized using various physicochemical techniques such as XRD, SEM, TEM and EDAX. XRD spectra of synthesized NPs confirmed the formation of CuO and Pd/Cu₂Cl(OH)₃. HRTEM analysis of CuO confirmed uniform cube-shaped morphology with particle size of 25–30 nm. Whereas, HRTEM of Pd/Cu₂Cl(OH)₃ showed 5–10 nm Pd NPs uniformly dispersed over Cu₂Cl(OH)₃ surface. Excellent catalytic activity was obtained for the conversion of benzaldehyde to methyl benzoate with 92% selectivity using Pd/Cu₂Cl(OH)₃ nanocatalyst. Other oxygenates such as aldehydes, alcohols and carboxylic acids were also obtained with high conversion and selectivity for desired methyl esters.

1. Introduction

Methylation of organic substrates is most fundamental as well as substantial transformation in synthetic organic chemistry, methyl group is one of the most significant functionality present on organic compounds [1]. Presence of methyl group greatly alters the pharmacological activity of biomolecules for multivarious biological phenomenon [2–6]. Conventionally frequently used methylating sources are methyl iodide, dimethyl sulfate, diazomethane, methyl carbonate and several methyl organometallic reagents [7]. The major class of methylations, that is, C-, N- and O-methylation have been investigated by the researchers. C-methylation includes methylation of aryl and vinyl halides, methylation of C–H bond, decarboxylative methylation of α , β -unsaturated compounds. N- and O-methylation includes methylation of N-containing compounds and O-methylation includes methylation of carboxylic acid [1].

Amongst all O-methylation of alcohols, aldehydes and carboxylic acids to produce their respective methyl esters results in the synthesis of the significant class of chemical compounds and building block in different natural product and polymers. Methyl esterification is one of the most fundamental transformations in organic synthesis [8,9]. There are several naturally occurring biologically active methyl esters such as

methyl jasmonate and biphenyl dicarboxylate which have medicinal applications. Fatty acid methyl esters are another significant class of versatile chemicals having potential applications in lubricants, metal working fluids, solvents fuels, surfactants, polymers, coatings and food. These fatty acid methyl esters are also used as “green solvents” because they are biodegradable, non-toxic and produce low volatile organic compounds (VOCs).

The common synthetic routes to methyl esters are the reactions of alcohols, aldehydes, acids with methanol in the presence of acid or base [7,10,11]. Mechanistically, the oxidation of hemiacetal intermediate, *in-situ* generated from the condensation of alcohol with aldehyde, is the key step for these conversions [12–15]. Transition metals such as Al, Au, Ru, Ir or Zn show high catalytic efficiency for the cross-esterification reaction of these organic substrates [16–19]. The Tishchenkoreaction of direct conversion of aldehydes to the corresponding esters represents the most effective method for the synthesis of esters. However, above said reactions results in the generation of undesired side products such as acids and alcohols with a very limited substrate scope [20]. Methyl esterification can also be synthesized by C–H functionalization resulting into C–O bond formation in presence of CO and methanol [21], C–H activation of alkoxy carbonylation of aryl (C–H sp^2), alkenyl (C–H sp^2), alkynyl (C–H sp), alkyl (C–H sp^3) with methanol and other

* Corresponding author at: Discipline of Chemistry, Indian Institute of Technology Indore, Simrol, Khandwa Road, Indore 453552, India.
E-mail address: xray@iiti.ac.in (S.M. Mobin).

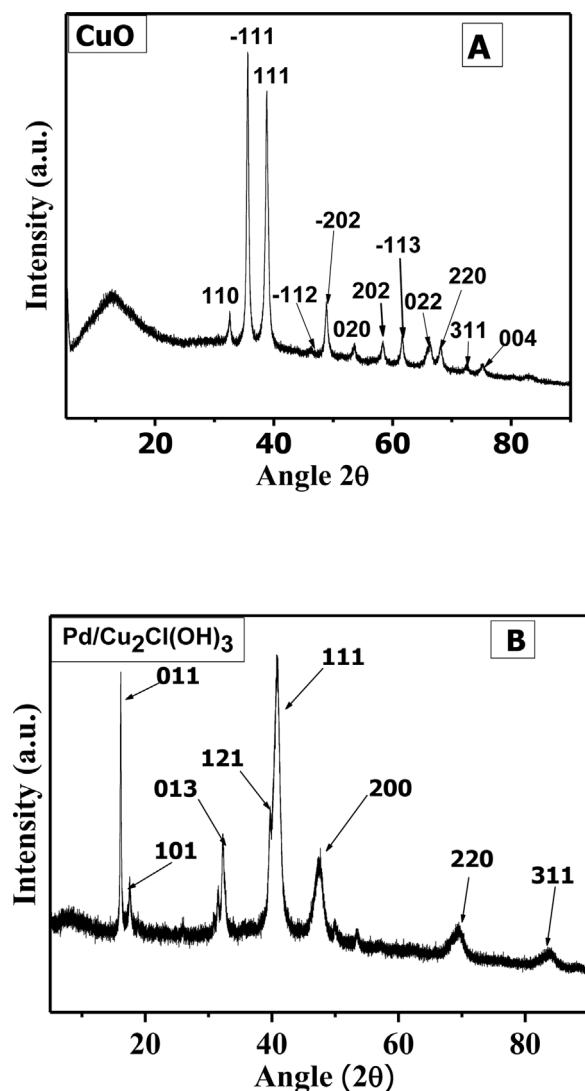
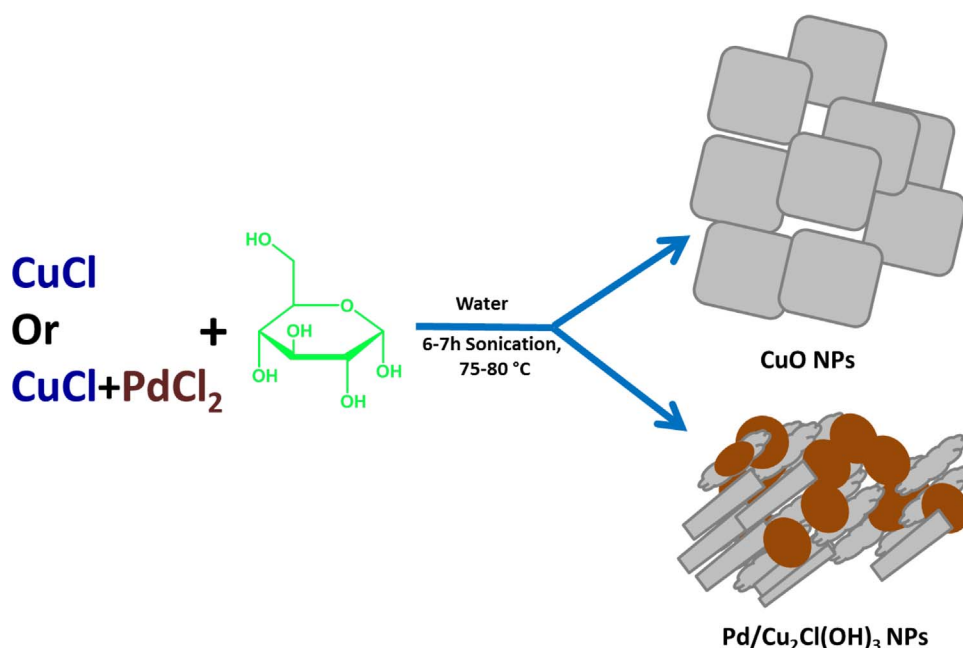


Fig. 1. XRD spectra of CuO NPs (A); Pd/Cu₂Cl(OH)₃ NPs (B).

esterifying agents such as methyl chloroformate [22], α -ketoesters [23], CO₂ [24] and activation of alkenes with methyl formate via C–H activation of methyl formate etc. has been used extensively for esterification reaction. Hydroacylation of carbonyl compounds via aldehydic C–H bond activation with methanol has also been investigated for methyl esterification reaction [8]. Stereoselective alkoxycarbonylation of unactivated C(sp³)–H bond with alkyl chloroformates using Pd(II)/(IV) catalysis has been performed for esterification reaction [25]. To the best of our knowledge, there are very few examples of Cu-catalyzed direct esterification of alcohols, aldehydes, carboxylic acid with tert-Butyl hydroperoxide as oxidant as well as the methylating agent. Mao *et al.* [26] have reported methyl esterification using TBHP as oxidant and C-methylating agent and Cu-quinoline complex as a catalyst and tetrabutylammonium iodide (TBAI) as an additive. But, the aforementioned catalytic systems are not recyclable and uses toxic solvents such as N, N-dimethylformamide (DMF) or dimethylsulfoxide (DMSO). Li *et al.* [7] have investigated aforementioned reaction using copper fluoride (CuF₂) as a catalyst for oxidative methyl esterification. However, both the aforementioned protocols utilize homogeneous Cu-based catalyst and TBAI as an additive used resulting in the generation of the cupious amount of waste materials. Recently, there is also a report on the application of Cu-MOF as an effective heterogeneous catalyst for methyl esterification reaction. However, synthesis of such MOFs is complicated, therefore a benign protocol for synthesis of methyl ester using TBHP as a methylating as well as the oxidizing agent is a need of the hours [27].

To address the aforementioned issue, the present work demonstrates a step ahead for more a facile approach for chemical manufacturing by employing Cu-nanocatalyst for oxidative methyl-esterification reaction. The common applications of copper or copper oxide NPs revolves around four types of chemical reactions, namely reduction, hydrolysis, condensation, and oxidation [28]. On the basis of the previous literature reports, the methods for synthesizing CuO NPs can be classified as (a) chemical, [29] (b) electrochemical, [30] (c) photochemical, [31] (d) sonochemical, [32]. and (e) thermal treatment method [33]. The chemical treatment method is most frequently utilized and is further classified into wet chemical, [34] microwave assisted, reverse micelle [35] and ionic liquid assisted [36] methods depending on materials, reaction environment and synthetic methodology used. “Wet chemical” technique is long established method mostly involves reduction of metal salts such as copper(II) acetylacetonate, CuCl₂, Cu(NO₃)₂, etc. in

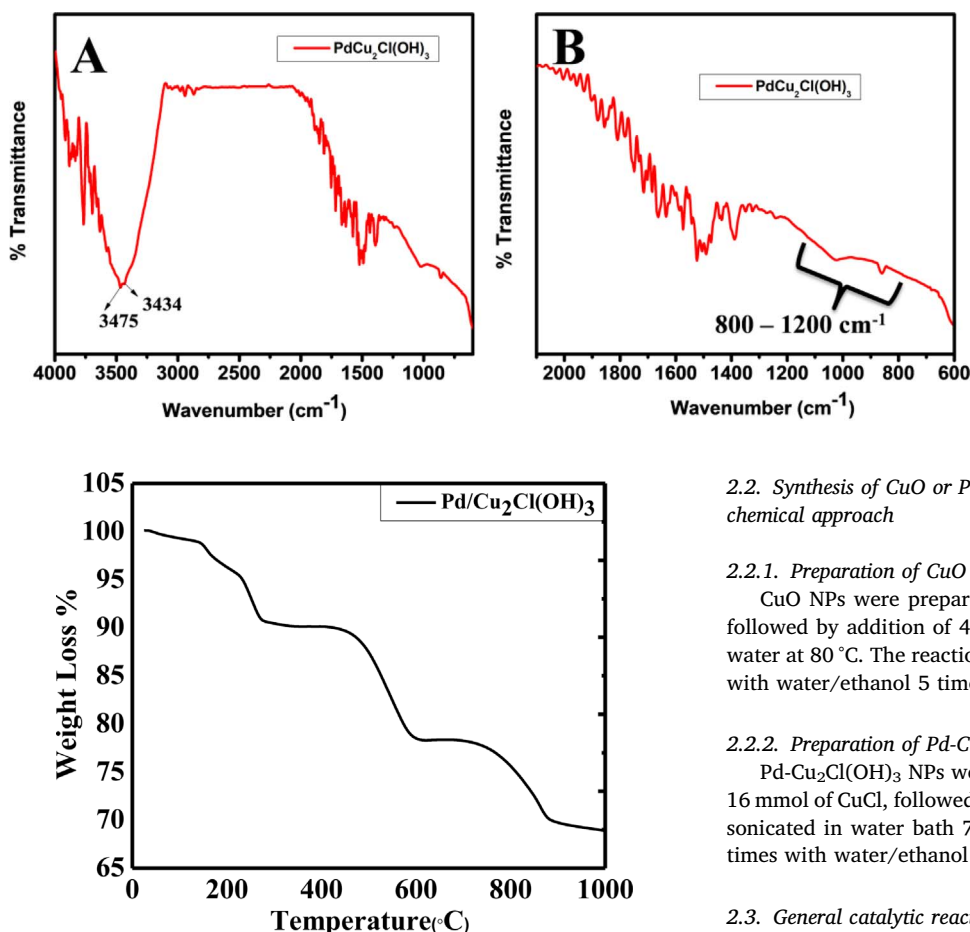


Fig. 3. Thermogravimetric analysis of as-prepared nanoscaled $\text{Pd/Cu}_2\text{Cl(OH)}_3$ (total sample weight: 6.541 mg).

presence of solvent; reducing agents sodium borohydride [37], hydrazine [38], ascorbic acid [39], D-glucose [40] etc.

There are several reports for the “wet chemical reduction” of cupric salts to metallic copper, Cu_2O or CuO NPs. Herein, the present manuscript we utilize “Wet chemical” method for synthesis of CuO NPs via oxidation of copper(I) chloride (CuCl) using dextrose as oxidizing agent and water as “green solvent”. Green, eco-friendly and benign method following 12 principles of green chemistry have been exhaustively addressed in this work by using water as “green solvent” and dextrose as renewable eco-friendly redox agent [41–43]. Replacement of hazardous organic solvents with water benign solvents, and renewable materials such as dextrose are key issues in the nanomaterials science field while considering a green synthetic strategy. The prime objectives of the present work is to use green, eco-friendly and more benign approach to the oxidative methyl-esterification reaction using robust, heterogeneous and recyclable copper based nanocatalyst. The present catalyst also has an edge over earlier reported catalyst in terms of homogeneous, non-recyclable, toxic solvents or catalytic material and complicated synthesis route.

2. Experimental

2.1. Materials

Commercially available starting materials were used as received. CuCl and dextrose were purchased from Merck India. Organic alkene, aldehydes, acids and alcohols were reagent purchased from Sigma Aldrich and other reagent grade solvents were used as received.

Fig. 2. FT IR spectra of $\text{Pd/Cu}_2\text{Cl(OH)}_3$ (A); $\text{Pd/Cu}_2\text{Cl(OH)}_3$ (B).

2.2. Synthesis of CuO or $\text{Pd-Cu}_2\text{Cl(OH)}_3$ nanoparticles (NPs) via wet chemical approach

2.2.1. Preparation of CuO NPs

CuO NPs were prepared by dissolving 16 mmol of CuCl (1.584 g), followed by addition of 4.0 g dextrose in 100 ml of distilled deionized water at 80 °C. The reaction was continued for 7 h followed by washing with water/ethanol 5 times and water 5 times.

2.2.2. Preparation of $\text{Pd-Cu}_2\text{Cl(OH)}_3$ NPs

$\text{Pd-Cu}_2\text{Cl(OH)}_3$ NPs were prepared by dissolving 4 mmol PdCl_2 and 16 mmol of CuCl , followed by addition of 4.0 g dextrose in 100 ml water sonicated in water bath 75–80 °C upto 6 h, centrifuged and washed 5 times with water/ethanol and 5 times with water.

2.3. General catalytic reaction

The liquid phase catalytic oxidation was carried out in a (50 ml one necked) round bottom flask equipped with a magnetic stirrer and immersed in a thermostat controlled oil bath. The flask was charged with substrate (1 mmol), oxidant TBHP 70 wt% in H_2O , 700 mg (8 eq), 10 mg of catalyst, K_2CO_3 (44 mg) and solvent acetonitrile: water (3:1) 4 ml. All the reactions were carried out at 100 °C, 24 h. Samples were periodically withdrawn and analyzed on Shimadzu GC–MS (Spectra S1–S23).

2.4. Physio-chemical characterizations

Powder X-ray diffraction studies were carried out on Rigaku SmartLab X-ray diffractometer using $\text{CuK}\alpha$ radiation (1.54 Å). Infrared spectra were performed with a Bio-Rad FTS 3000MX instrument using KBr pellets. Thermogravimetric analysis (TGA) were performed on METTLER TOLEDO (TGA/DSC 1) using software STAR^e System. H_2 -TPR analysis and CO titration was carried out in (Quantachrome). Temperature-programmed reduction (TPR) was performed in a micro-flow reactor (Quantachrome, Autosorb iQ2). To carry out the experiment, a catalyst sample (175 mg) was heated from 50 °C to 600 °C at a rate of 10 °C/min and fed with 80 ml/min of gas mixture containing 5% H_2 and 95% N_2 . CO titration was carried out on Quantachrome, Autosorb iQ2 to analyze the Pd dispersion on the catalysts surface using carbon monoxide as the adsorbate and Pd as the adsorbent at ambient temperature and pressure. FE-SEM attached with EDAX was done using Supra55 Zeiss Field-Emission Scanning Electron Microscope. Transmission Electron Microscopy was carried on FEI Tecnai G2 12 Twin TEM. XPS analysis of fresh and spent catalyst ($\text{Pd/Cu}_2\text{Cl(OH)}_3$) was performed using X-ray Photoelectron Spectroscopy (XPS) with Auger Electron Spectroscopy (AES) Module: Model/Supplier: PHI 5000 Versa Prob II, FEI Inc. Identification of the products of the carried out using Shimadzu GC–MS equipped with QP2010 mass spectrometer and RTX-5 tubular diphenyl dimethyl polysiloxane

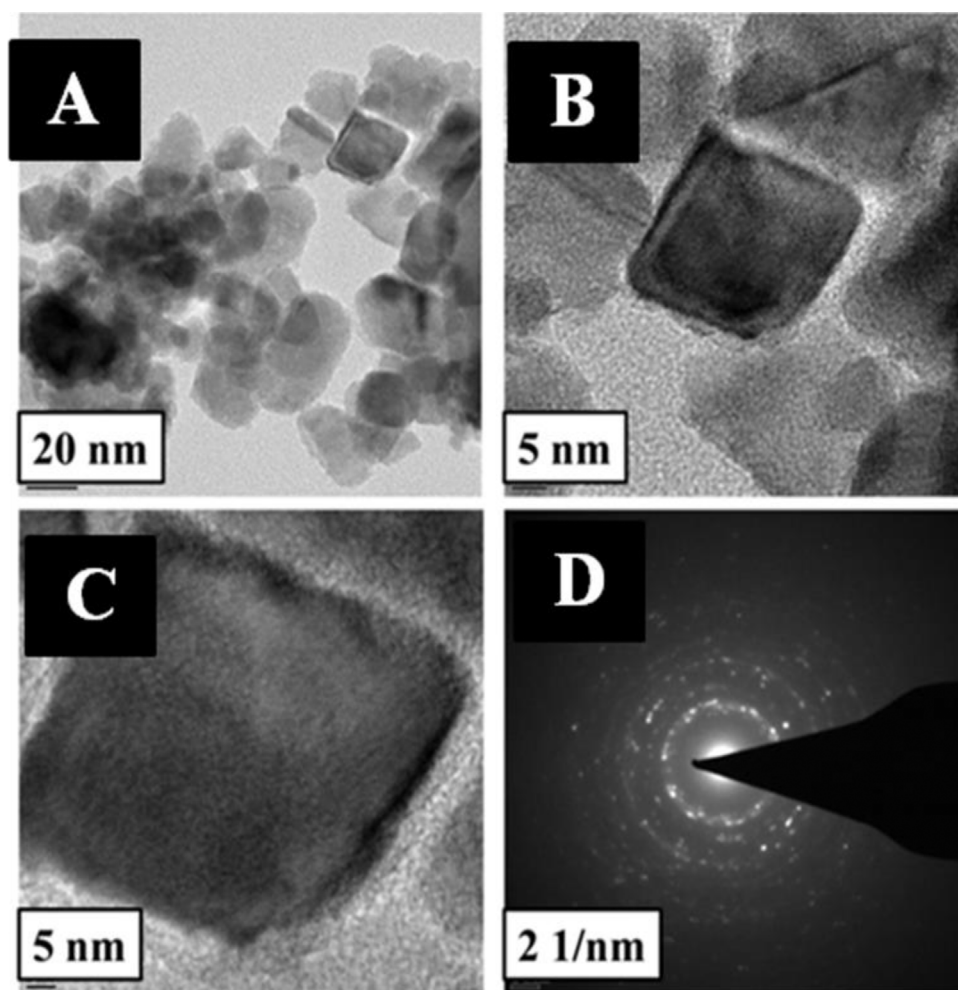


Fig. 4. HRTEM image of CuO nanocatalyst at 20 nm (A); 5 nm (B); 5 nm (C) magnification; SAED pattern of CuO nanocatalyst at 2 1/nm (D).

capillary column 30 m long, 0.25 mm diameter and df value of 1.0 μm .

3. Results and discussion

3.1. Characterization of the catalytic materials

Synthesis of copper oxide and Cu-Pd based nanoparticles (NPs) were carried out using “wet chemical method” as shown in Scheme 1.

$$B(2\theta) = \frac{K\lambda}{L \cos \theta}$$

The XRD patterns of CuO NPs showed the monoclinic structure with $2\theta = 32.1^\circ, 35.2^\circ, 39.1^\circ, 48.3^\circ, 58.2^\circ, 62^\circ, 66.2^\circ, 68.3^\circ$ and 75.2° which can be readily indexed as 100, 11-1, 111, 200, 20-2, 002, 113, 220 and 311 planes, respectively (Fig. 1A) [44]. Particle size was calculated using Scherrer's equation.

Particle size of the CuO nanoparticles calculated using Scherrer's equation was found to be 30 nm. The XRD pattern of Pd-nanoparticles supported on copper based NPs [Pd/Cu₂Cl(OH)₃] is shown in Fig. 1B. The observed intense Bragg reflection peaks at $40.9^\circ, 47.9^\circ, 69.4^\circ, 84.2^\circ$ and 87° representing the 111, 200, 220, 311 and 222 respectively, was compared and confirmed the formation of palladium NPs (JCPDS standard 05-0681) [45,46]. Moreover, the four main diffraction peaks at $2\theta = 16.4^\circ, 32.1^\circ, 39.6^\circ$ and 50.3° are ascribed to the phase of chinoatcamite Cu₂Cl(OH)₃ (JCPDS 50–1559) (Fig. 1B) [47]. Particle size of Pd/Cu₂Cl(OH)₃ calculated using Scherrer's equation was found to be 12 nm.

In the FT-IR spectrum of Pd/Cu₂Cl(OH)₃ (Fig. 2), the two absorption

peaks at 3447 and 3358 cm^{-1} are ascribed to the hydroxyl stretching modes $\nu_1(\text{O1-H1})/\nu_1(\text{O2/3-H2/3})$ of the Cu₂Cl(OH)₃, the IR bands between 800–1200 cm^{-1} can be attributed to the δ_1 and ν_1 (Cu–O–H) vibrations [48].

Thermogravimetric analysis (TGA) was performed to determine thermal characterisation of Pd/Cu₂Cl(OH)₃ (Fig. 3). Here, decomposition of Pd/Cu₂Cl(OH)₃ is observed with 9.5 wt% (0.621 mg) weight-loss below 300 $^\circ\text{C}$, followed by 12 wt% (0.784 mg) up to 600 $^\circ\text{C}$ and finally 9.3% (0.61 mg) weight loss from 600–900 $^\circ\text{C}$. This weight loss is due to the dissociation of HCl and water molecules [49]. XRD, FT IR and TGA analysis corroborate formation of Cu₂Cl(OH)₃ in Pd/Cu₂Cl(OH)₃ [47–50].

SEM micrograph shows uniformly dispersed CuO and Pd-Cu₂Cl(OH)₃ NPs (Fig. S1 (A–D)). EDAX analysis of Pd-Cu₂Cl(OH)₃ is shown in Fig. S2 A–F, Table S1. The EDX spectrum obtained from samples indicated that Pd/Cu₂Cl(OH)₃ nanoparticles contain the elemental Pd, Cu, O and Cl [48]. EDX analysis shows that the atom ratio of Cu and Cl is nearly 2:1, indicating that the composition of the as-prepared samples is Cu₂Cl(OH)₃ (Table S1). EDAX analysis confirms the presence of Pd, Cu and Cl in Pd-Cu₂Cl(OH)₃ [Fig. S2 (A–F) and Table S1]. HRTEM image of CuO NPs also reveals the formation of uniformly dispersed size and cube-shaped NPs of 30–40 nm dimensions (Fig. 4). Selected area electron diffraction (SAED) performed on samples of CuO NPs aggregate obtained from HR-TEM showed a concentric ring pattern indicating crystalline nature of the material (Fig. 4). HRTEM images of Pd-Cu₂Cl(OH)₃ NPs are presented in (Fig. 5). HRTEM of as-prepared NPs show formation of uniformly dispersed Pd NPs (10–15 nm) over Cu₂Cl(OH)₃ surface (Fig. 5A–C). SAED pattern of Pd-Cu₂Cl(OH)₃

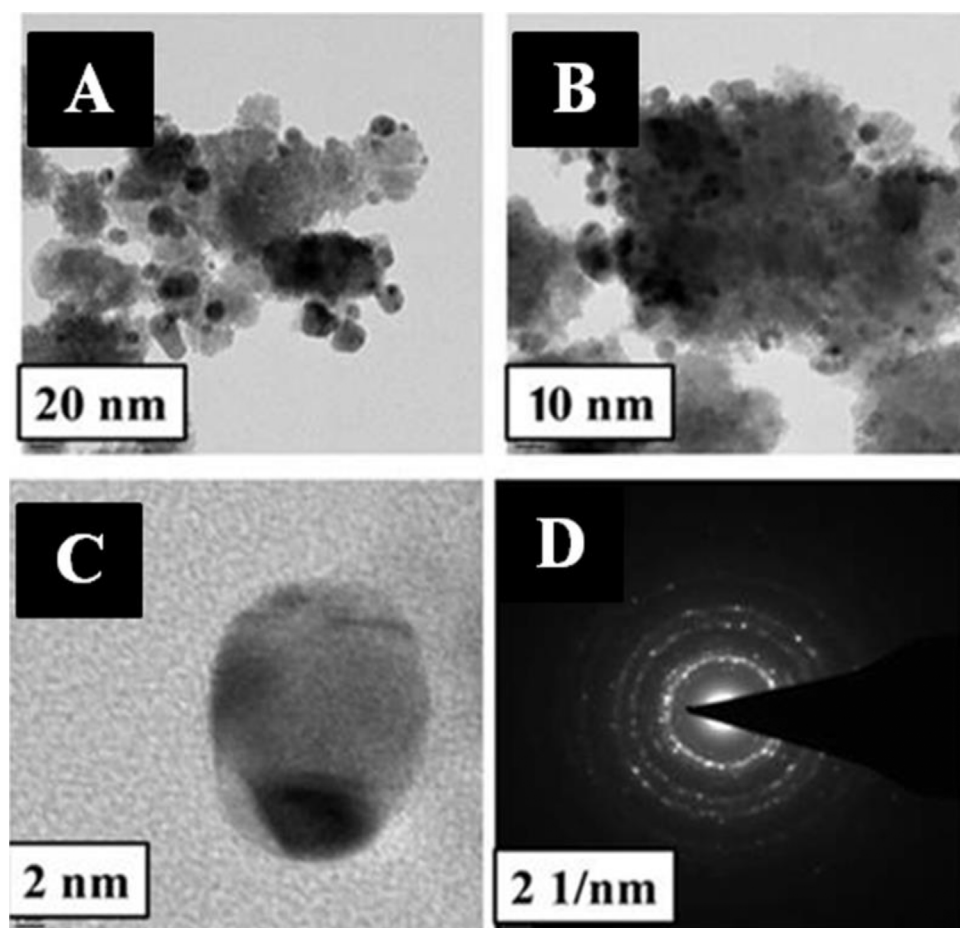


Fig. 5. HRTEM image of Pd-Cu₂Cl(OH)₃ nanocatalyst at 20 nm (A); 10 nm (B); 2 nm; (C) SAED image of Pd-Cu₂Cl(OH)₃ nanocatalyst at 2 1/nm (D).

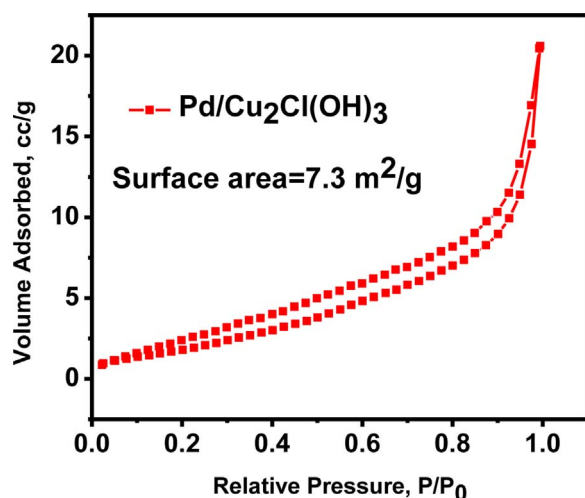


Fig. 6. Brunauer–Emmett–Teller (BET) surface area of the Pd/Cu₂Cl(OH)₃.

presents concentric rings revealing formation of crystalline material (Fig. 5D).

The Brunauer–Emmett–Teller (BET) surface area and pore diameters of the Pd/Cu₂Cl(OH)₃ were determined by N₂ adsorption measurements (see. Surface area of the catalyst calculated from BET measurements was 7.3 m²/g. (Fig. 6). To determine the presence of Pd nanoparticles on the catalyst surface SEM-EDAX analysis was performed and confirmed the presence of Pd atoms on the catalyst surface [See Fig. S2 (F) and Table S1].

CO titration was also performed to analyze the Pd dispersed over the

Cu₂Cl(OH)₃ surface. CO titration study reveal that surface area of Pd dispersed over Cu₂Cl(OH)₃ have surface area 1.04 m²/g with average crystallite size of 182.5 nm. As for the well-reduced Pd/Cu₂Cl(OH)₃ show particle sizes were estimated by CO chemisorptions under the assumption that CO was linearly adsorbed on Pd/Cu₂Cl(OH)₃ surface and the estimated sizes were actually larger than the particle size monitored using TEM or XRD due to surface carbonyl formation with more than one CO molecule being adsorbed per surface Pd atom [51].

The high-resolution XPS spectra in Fig. 7 and 8 reveal the survey of the fresh and spent Pd-Cu₂Cl(OH)₃ nanocatalysts. High resolution XPS spectra of Pd-region reveals a doublet structure each with two pairs of peaks at 335.6 and 340.9 eV representing Pd 3d_{3/2} and Pd 3d_{5/2}, respectively for bulk Pd(0) (Fig. 7A–B) [48]. The Cu 2p peak XPS spectrum (Fig. 7A–C) shows the two peaks centered at 933 and 953 eV were assigned to Cu 2p_{3/2} and Cu 2p_{1/2} present in Cu₂Cl(OH)₃. XPS spectra of spent catalyst was identical clearly indicated that there was no change in oxidation state of Cu²⁺ in both fresh and spent catalyst after five recycles (Fig. 8A–C).

H₂-temperature programmed reduction profile for Pd/Cu₂Cl(OH)₃ show presence of two broad peaks between 50 and 200 °C in their TPR digram, assigned to reduction of Pd (Pd²⁺ to Pd). Earlier reports suggest it is due to the reduction of different PdCu species [52–54]. Also peaks between 100 and 200 °C and a small peak between 200 and 250 °C are assigned to α- and β- peaks due to highly dispersed CuO nanoparticles. Third peak which is extended between 300 and 400 °C corresponds to the reduction of Cu²⁺ to Cu as shown in Fig. S3[52–55].

3.2. Catalytic results

Catalytic methyl- esterification of alcohols, aldehydes and carboxylic acids were carried out using tert-butylhydroperoxide (TBHP) as

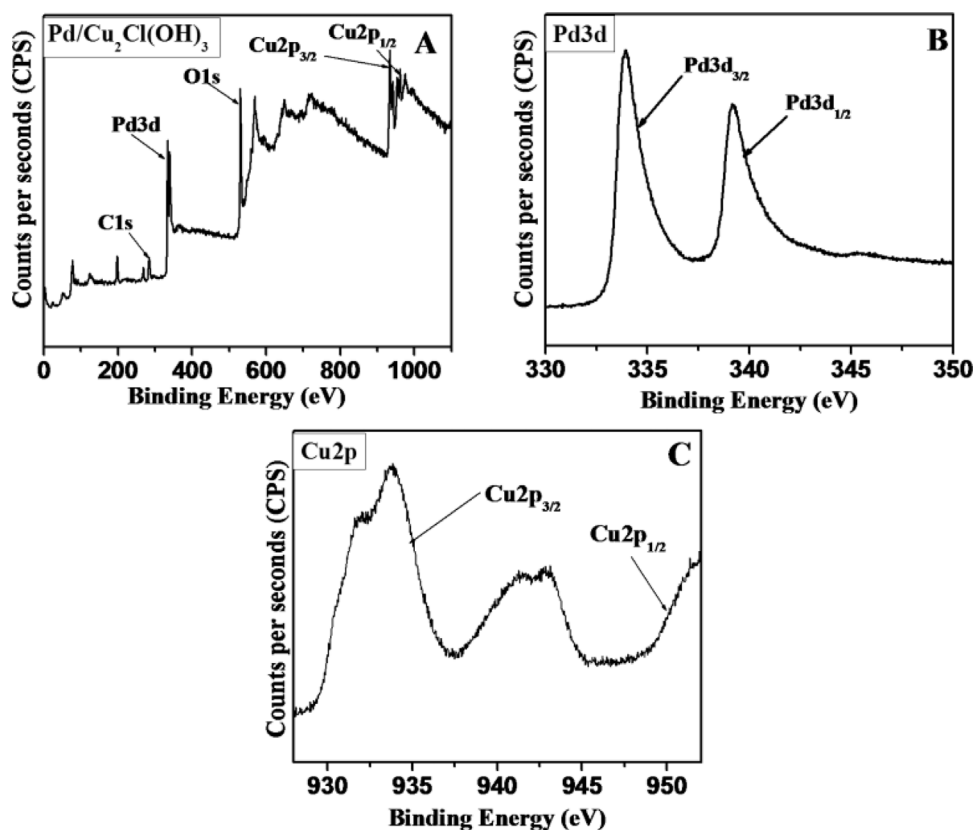


Fig. 7. XPS spectra of survey spectrum of fresh Pd- $\text{Cu}_2\text{Cl}(\text{OH})_3$ (A); Pd 3d (B); Cu 2p (C).

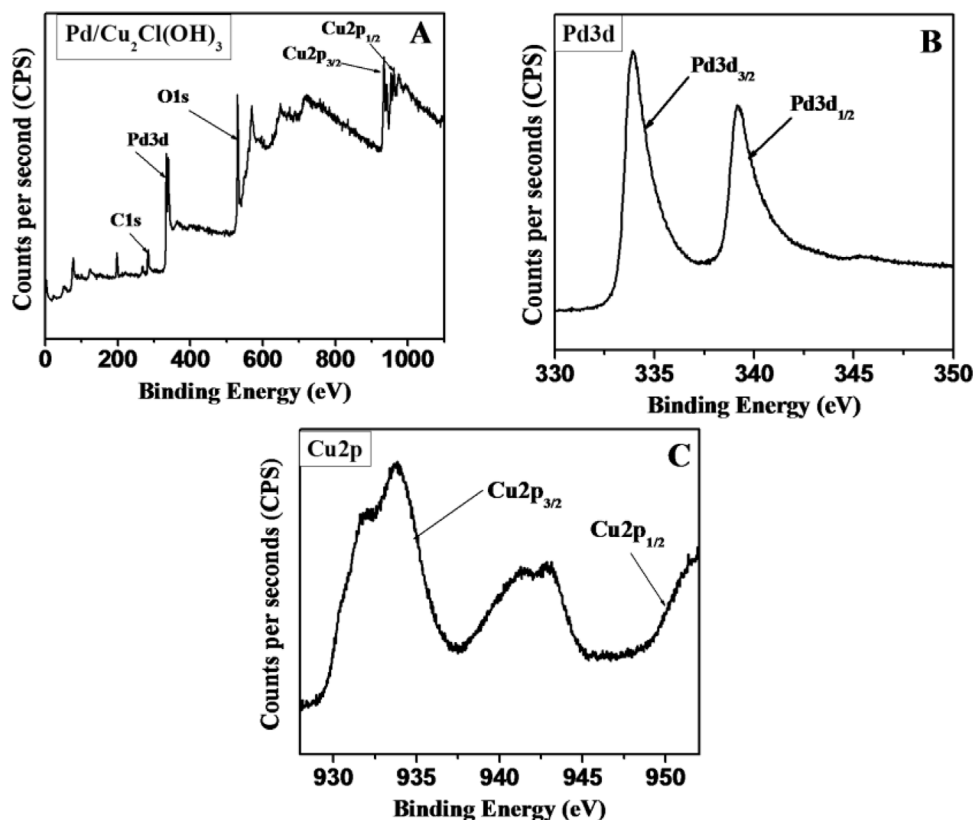
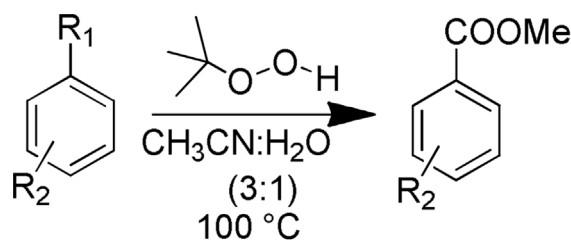


Fig. 8. XPS spectra of survey spectrum of spent Pd- $\text{Cu}_2\text{Cl}(\text{OH})_3$ (A); Pd 3d (B); Cu 2p (C).

oxidizing as well as methylating agents in presence of acetonitrile:water (3:1) as solvent at 100 °C. PdCl_2 , CuCl , $\text{PdCl}_2 + \text{CuO}$ were employed as catalytic materials for methyl esterification reaction (Scheme 2 and

Table 1 and 2). Catalytic methyl-esterification of (4-methoxyphenyl) methanol using CuCl as catalyst resulted in complete conversion of the substrate with the formation of methyl-4-methoxybenzoate major



$R_1 = \text{CH}_2\text{OH}$

$R_2 = \text{H, Cl, OMe, and iso-propyl}$

$R_1 = \text{CHO}$

$R_2 = \text{H, Br, NO}_2, \text{OH, Cl, OMe and CN}$

$R_1 = \text{COOH}$

$R_2 = \text{H and NO}_2$

Scheme 2. Catalytic methyl-esterification of alcohols, aldehydes and acids using PdCl_2 , CuCl , $\text{PdCl}_2 + \text{CuO}$, CuO or $\text{Pd-Cu}_2\text{Cl}(\text{OH})_3$ nanocatalyst and TBHP as oxidizing and methylating agent.

Table 1
Screening of catalysts for methyl-esterification of (4-methoxyphenyl)methanol.

Entry	Catalyst	% Conv.	% Selectivity		
			A	B	C
1 ^a	CuCl	100	66	–	34
2 ^b	PdCl_2	100	27	26	47
3 ^c	$\text{PdCl}_2\text{-CuO}$	99.5	43	45	12

product with 66% selectivity. PdCl_2 under identical conditions gave 4-methoxybenzoic acid and methyl 4-methoxybenzoate were formed with 26% and 27% selectivity respectively. To determine the role of Pd^{2+} and Cu^{2+} in the catalytic reaction, PdCl_2 (4 mg with respect to (4-methoxyphenyl)methanol) and CuO (6 mg with respect to (4-methoxyphenyl)methanol) were used as catalyst for aforementioned reaction. 4-methoxybenzoic acid was formed as major product with 45% selectivity. 4-methoxybenzoate was formed as major byproduct with 43% selectivity.

Furthermore, as discussed in the previous sections CuO and $\text{Pd-Cu}_2\text{Cl}(\text{OH})_3$ were used for oxidation of (4-methoxyphenyl)methanol to investigate the role of Pd. Catalytic methyl esterification was carried out using (4-methoxyphenyl)methanol because electron rich benzyl alcohol is the best substrate for methyl-esterification because electron donating group help in stabilizing the $\text{PhCOO}\cdot$ free radical, resulting in enhance reactivity with methyl free radical generated during the reaction. Therefore, electron rich benzyl alcohol is best substrate for methyl esterification. In presence of CuO nanocatalyst (4-methoxyphenyl)methanol showed 100% conversion with 70% selectivity for methyl 4-methoxybenzoate whereas in presence of $\text{Pd-Cu}_2\text{Cl}(\text{OH})_3$ nanocatalyst 4-methoxy benzyl alcohol completely converted to methyl 4-methoxybenzoate with 96% selectivity for methyl 4-methoxybenzoate. Thus, further the substrate scope was investigated using $\text{Pd-Cu}_2\text{Cl}(\text{OH})_3$ nanocatalyst. To examine the scope of methyl esterification reaction several substituted benzylic alcohols were also investigated for the synthesis of methyl esters. The results are summarized in Table 2. $\text{Pd-Cu}_2\text{Cl}(\text{OH})_3$ nanocatalyst tolerated several steric and electronic substituents of the benzylic alcohols, as well as heterocyclic substrates, all resulting in moderate to excellent yield. Benzaldehyde and substituted

Table 2

Catalytic methyl-esterification using TBHP as methylating source and oxidizing agent using $\text{Pd/Cu}_2\text{Cl}(\text{OH})_3$ heterogeneous catalyst.

Entry	Substrate	% Conv.	(Methyl ester)	% Sel.
Alcohols				
1		100		96
2*		100		70
3		100		93
4		100		72
5		100		71
6		98		44
Aldehydes				
7		100		100
8		100		93
9		100		87
10		100		87
11		100		92
12		100		85

(continued on next page)

Table 2 (continued)

Entry	Substrate	% Conv.	(Methyl ester)	% Sel.
Alcohols				
13		100		64
14		100		41
15		100		30
Carboxylic acids				
16		100		97
17		100		92
18		100		100
Miscellaneous				
19		100		40
20		100		34
21		49		65

benzaldehyde also showed excellent yields for their respective methyl esters. A wide range of functional groups, including –Br, –Cl, cyano, and nitro, all were performed smoothly under the optimized conditions. 2-Hydroxy benzaldehyde showed 30% yield for the corresponding methyl ester. Lower yield for hydroxyl substituted benzaldehyde may be due to its sensitive nature towards oxidants present in the substrate. After the successful application of the oxidative methyl esterification of the alcohols and aldehydes, this methodology was utilized for carboxylic acid since they are cheaper and stable. The benzoic acid and substituted benzoic acids showed better catalytic performance corresponding to alcohols and aldehydes under identical reaction conditions. Five and six-membered heterocyclic compounds were also investigated for methyl-esterification reaction. Pyridin-2-yl methanol under identical reaction condition gave 100% conversions and 40% selectivity for desired methyl picolinate. Benzo[d][1,3]dioxol-5-ylmethanol showed 100% conversion but only 30% selectivity for desired methyl benzo[d][1,3]dioxole-5-carboxylate. Furan-2-carbaldehyde showed 49% conversion and 65% selectivity for methyl furan-2-carboxylate. Alcohols containing heterocyclic moieties were comparatively less active as

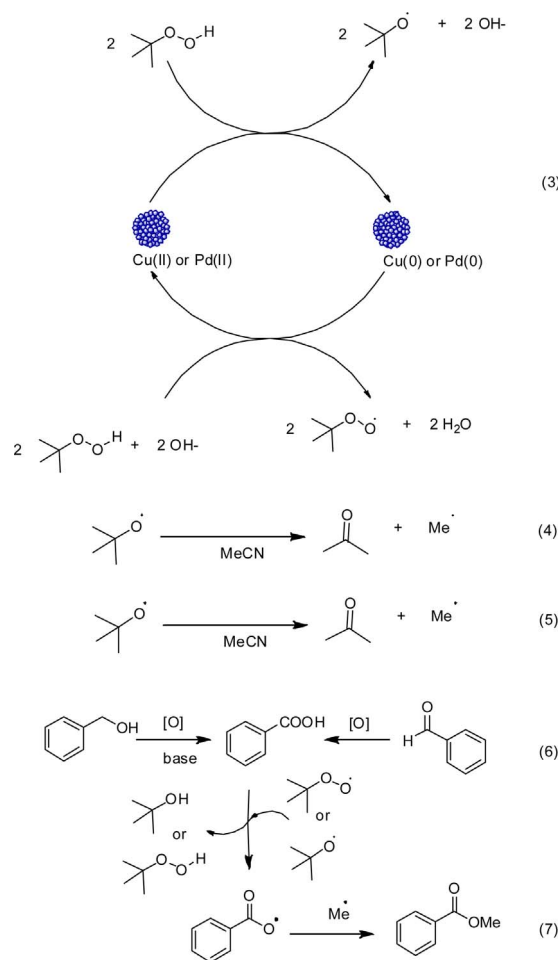


Chart 1. Mechanism for methyl-esterification of benzyl alcohols using CuO or Pd-Cu₂Cl(OH)₃ nanocatalyst and TBHP as an oxidizing and methylating agent.

compared to non-heterocyclic moieties because they have the tendency to bind to transition metals and can act as catalyst deactivators. Therefore, heterocyclic moieties gave the inferior catalytic performance with Pd/Cu₂Cl(OH)₃ catalyst.

Reaction conditions: 1 mmol of (4-methoxyphenyl)methanol; 700 mg (8 equivalent) TBHP (70 wt% in H₂O); CuCl (10 mg with respect to (4-methoxyphenyl)methanol); PdCl₂ (10 mg with respect to (4-methoxyphenyl)methanol); PdCl₂:CuO (4 mg PdCl₂: 6 mg CuO with respect to with respect to (4-methoxyphenyl)methanol); K₂CO₃ (44 mg) in 4 ml CH₃CN:H₂O (3:1) heated in 100 °C; time = 24 h, A = methyl-4-methoxybenzoate; B = 4-methoxybenzoic acid; C = others; products were confirmed by GCMS.

Reaction conditions: 1 mmol of substrate; 700 mg (8equivalent) TBHP (70 wt% in H₂O); Pd-Cu₂Cl(OH)₃(10 mg),* CuO (10 mg); K₂CO₃ (44 mg) in 4 ml CH₃CN:H₂O (3:1) heated in 100 °C; time = 24 h, products were confirmed by GCMS.

3.3. Mechanistic insight into the catalytic methyl esterification

Based on previous literature reports the most plausible mechanism for methyl esterification of organic substrates by using Cu- or Pd-Cu₂Cl(OH)₃ based catalysis is illustrated in Chart 1 [26]. Cu²⁺ presents better catalytic performance as compared to other support because Cu²⁺ is a superior oxidizing agent with the standard oxidation potential of +0.34 eV. Pd²⁺ is still the strong oxidizing agent with the standard oxidation potential of +0.951 eV [56]. Therefore, incorporation of Pd²⁺ to the catalytic material further enhances the catalytic performance towards oxidative methyl esterification reaction. The reaction

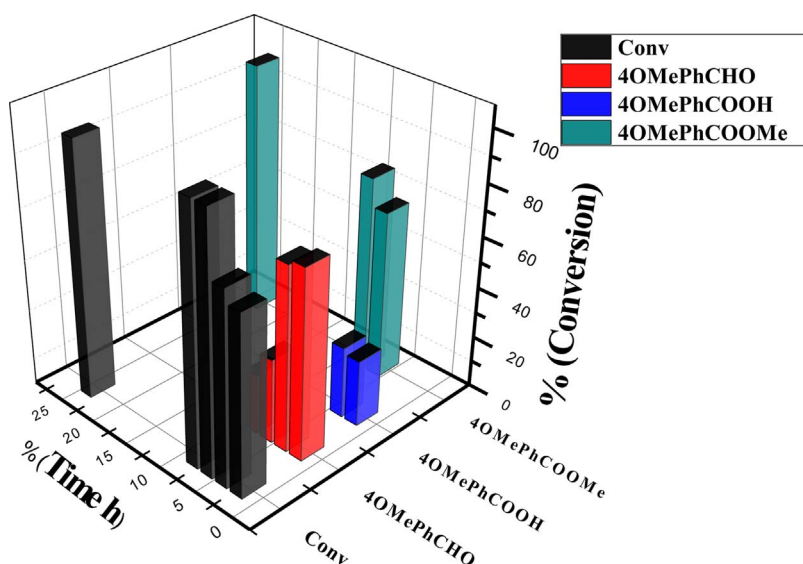


Fig. 9. Kinetic study for catalytic methyl-esterification of 4-OMe-PhCH₂OH.

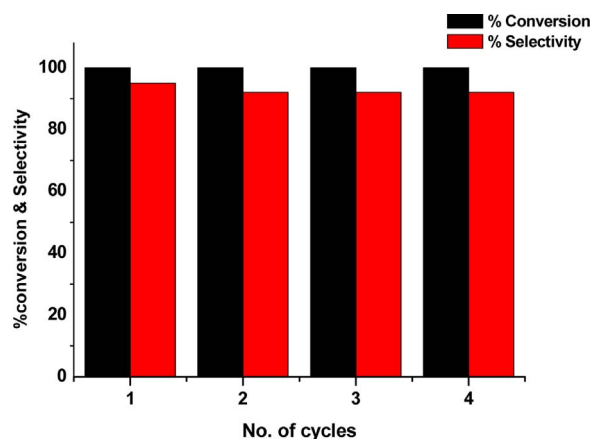


Fig. 10. Recycle study for methyl esterification of (4-methoxyphenyl)methanol using Pd-Cu₂Cl(OH)₃ nanocatalyst and TBHP as an oxidizing and methylating agent.

initiates with the decomposition of TBHP to generate the *tert*-butoxyl and *tert*-butylperoxy radicals in the presence of Cu or Pd-Cu₂Cl(OH)₃ catalyst [57,58]. The alcohols and aldehydes directly oxidized carboxylic acid in the presence of oxidant, base and CuO or Pd-Cu₂Cl(OH)₃ nanocatalyst. TBHP is activated by Pd or Cu ions present in Pd-Cu₂Cl(OH)₃ nanocatalyst to form *tert*-butoxyl or *tert*-butylperoxy radicals. *In-situ* generated *tert*-butoxyl radical is converted by a simplistic unimolecular mechanism to acetone and a methyl radical [59]. Previously Hix et al. [60] have performed EPR studies to investigate methyl esterification of DNA molecule to form methylated DNA molecule using TBHP molecule as oxidizing agent and methyl source. EPR studies clearly show formation of methyl free radical. They also detected formation of acetone during the reaction. Eventually, the carboxylic acid reacts with *in-situ* generated *tert*-butoxyl or *tert*-butylperoxy radical to form acyloxy radical. The acyloxy radical ultimately reacts with methyl radical resulting into the desired ester.



3.4. Kinetic and recycle study

Kinetic study for catalytic methyl-esterification of 4-OMe-PhCH₂OH (4-methoxyphenyl)methanol) was performed by periodically injecting

the samples into the GC. Kinetic study experiments show complete conversion of 4-OMe-PhCH₂OH with 76.5% selectivity for methyl 4-methoxybenzoate in 8 h. However 4-OMe-PhCH₂OH was completely converted into methyl 4-methoxybenzoate in 24 h. Kinetic study for 4-OMe-PhCH₂OH methyl-esterification is shown in Fig. 9. Leaching study was performed by removing the catalyst from the reaction mixture after 1 h and then continuing the reaction for 24 h without catalyst. Leaching test was carried out using the hot filtration experiment. After 1 h, the reaction was stopped and the catalyst was removed from reaction media by centrifugation and supernatant was allowed to react further without catalyst. Catalyst leaching studies show dip in 4-OMe-PhCH₂OH (50%) conversion with 3.5% selectivity for methyl 4-methoxybenzoate and 50% selectivity for 4-OMe-PhCHO.

Reaction conditions: 1 mmol of substrate; 700 mg (8 equivalent) TBHP (70 wt% in H₂O); Pd-Cu₂Cl(OH)₃ (10 mg); K₂CO₃ (44 mg) in 4 ml CH₃CN:H₂O (3:1) heated in 100 °C; time = 24 h, products were confirmed by GCMS.

Pd-Cu₂Cl(OH)₃ NPs were also used to check the reusability for methyl esterification of methyl 4-methoxybenzoate. After each reaction cycle, the catalyst was separated by centrifugation and washed with solvent and used for next run. There was no considerable decrease in conversion of methyl 4-methoxybenzoate and methyl 4-methoxybenzoate was formed even after fourth recycle. (Fig. 10)

Reaction conditions: 1 mmol of substrate; 700 mg (8 equivalent) TBHP (70 wt% in H₂O); Pd-Cu₂Cl(OH)₃ (10 mg); K₂CO₃ (44 mg) in 4 ml CH₃CN:H₂O (3:1) heated in 100 °C; time = 24 h, products were confirmed by GCMS.

4. Conclusions

To summarize methyl-esterification of various substituted alcohols, aldehydes and carboxylic acids were carried out using *tert*-butylhydroperoxide (TBHP) which act as an oxidizing as well as the methylating agent using CuO or Pd/Cu₂Cl(OH)₃ nanocatalysts. CuO or Pd/Cu₂Cl(OH)₃ NPs were synthesized by wet chemical method of CuCl and PdCl₂ by using green solvent “water”. HRTEM of as-prepared CuO materials showed a cube-shaped NPs. HRTEM showed the formation of spherical Pd nanoparticles dispersed on Cu₂Cl(OH)₃ surface. Using more amount of substrates with less amount of nanocatalyst Pd/Cu₂Cl(OH)₃ showed excellent catalytic performance with high conversions and selectivity towards aldehydes, alcohols and carboxylic acids for their respective desired methyl esters.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.apcatb.2017.12.056>.

SEM;1;-EDAX, elemental mapping (Fig. S1-S3 and Table S1) and GC-MS data (Spectra:S1-S23) and NMR (Spectra: S24-25) can be accessed from supporting information.

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